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| PARKIN, JEFFREY S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 04/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/076,421 | WADA ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey S. Parkin, Ph.D. | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/01/02; 08/13/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## Detailed Office Action

### *Status of the Claims*

Applicants election of Group I (claims 1-5 and 8) with traverse in the response dated 21 January, 2004, is acknowledged. Since applicants did not distinctly and specifically point out the purported errors in the restriction requirement, the election has been treated as an election without traverse (refer to M.P.E.P. § 818.03(a)). Claims 6, 7, and 9-26 are withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

### *37 C.F.R. § 1.74*

The disclosure is objected to because it fails to comply with 37 C.F.R. § 1.74. The brief description of the figures is inadequate. For instance, figure one references four different constructs ((a)-(d)), yet the figure description only vaguely references a single figure. Figure 7 references experimental results, but fails to provide an even rudimentary description of the parameters being examined (for instance, what general scientific question does the figure address, which parameters are being measured, etc.). The description of the figures should be amended to include a more complete description.

### *Information Disclosure Statement*

The information disclosure statement filed 13 August, 2002, has been placed in the application file and the information referred to therein has been considered where indicated. The

information disclosure statement filed 01 November, 2001, fails to comply with 37 C.F.R. § 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

### *35 U.S.C. § 112, Second Paragraph*

Claims 4, 5, and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims reference a ligand binding molecule, identified simply as ATF, that is vague and indefinite since it fails to clearly identify the agent of interest. For instance, does this designation refer to an organic compound or polypeptide? If it refers to a polypeptide (i.e., the amino terminal fragment) the source of the peptide should clearly be identified and the amino acid residues encompassing the fragment set forth (i.e., the amino terminal fragment (ATF) of the high molecular weight urokinase-type plasminogen activator (HMW-uPA), wherein said fragment consists of amino acids 21-155, ...). The reference to a "specific binding affinity" for a ligand that is capable of binding to CD87 is confusing, since the precise binding characteristics are not clearly set forth. For instance, do the claims encompass a high binding affinity ($10^{-9}$ M) or low binding affinity ($10^{-2}$ M)? Appropriate correction is required.

### *35 U.S.C. § 112, First Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims are broadly directed toward any "anti-HIV" agent that encompasses a "ligand molecule binding to CD87". Accordingly, the claims can encompass a sundry number of structurally unrelated compounds such as proteins, analogues, polypeptides, antibodies, or peptidomimetics. However, the disclosure only identifies a single compound (HMW-uPA) and an amino terminal fragment (aa 21-155) of this compound with the desired activity. The disclosure does not provide any uPA analogues or other inhibitory compounds.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of sundry "anti-HIV" agents. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations

using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide

evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight. The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

As noted *supra*, the disclosure fails to identify suitable uPA analogues, or analogue fragments thereof, with the desired activity. Moreover, the disclosure fails to identify a single non-uPA molecule (i.e., antibody, receptor mimetic, trans-dominant mutant, peptidomimetic, organic compound, etc.) with the desired properties. The disclosure clearly fails to lead

the skilled artisan to any other compounds other than those disclosed in the specification. Applicants may obviate the rejection by directing the claim language toward HMW-uPA and ATFs of said protease.

Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. It is noted that the disclosure demonstrates that HMW-uPA and a specific ATF of said protease (aa 21-155) are capable of inhibiting HIV-1 infection. Appropriate amendment of the claim language to reflect this finding would be acceptable. However, the disclosure is clearly not enabled for the full breadth of protection directed toward any sundry "anti-HIV" agent that is capable of binding to CD87.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as

follows:

**1) The disclosure fails to identify the molecular determinants modulating ligand-CD87 receptor binding interactions.** In order to design rational antivirals, the skilled artisan would require a knowledge of those residues that are critical for binding to CD87, and how these interactions translate into anti-HIV activity.

**2) The disclosure fails to identify the molecular determinants modulating the antiviral activity of uPA.** In order for the skilled artisan to design suitable analogues, a knowledge of those regions of uPA that are critical for such activity needs to be clearly set forth. Otherwise, the skilled artisan is being asked to guess as to which regions are critical and which regions can tolerate amino acid substitutions, additions, deletions, or modifications.

**3) The disclosure fails to identify a reasonable number of "anti-HIV" ligands capable of binding to CD87.** The disclosure fails to identify and provide the structure of other compounds (i.e., antibodies, peptidomimetics, organic molecules, etc.) that display the requisite antiviral activity. The disclosure fails to set forth any salient structural information for any given inhibitor, other than uPA.

**4) The disclosure fails to demonstrate that uPA, or any other compound, are capable of inhibiting both HIV-1 and -2.** The claims are broadly directed toward an "anti-HIV" agent which encompasses agents that inhibit both HIV-1 and -2. However, the disclosure only describes a single protein, and fragment thereof, that are capable of inhibiting HIV-1, only. Although HIV-1 and -2 are both human immunodeficiency viruses, they display considerable genotypic heterogeneity and only display approximately 35% genetic relatedness. Thus, many HIV-1-specific agents fail to inhibit HIV-2, and vice versa.

**5) The disclosure fails to provide a sufficient number of working embodiments.** The claims are of considerable breadth and encompass analogues, antibodies, peptidomimetics, and small molecule inhibitors. However, the only working embodiments provided in the disclosure are directed toward uPA and the ATF of this protein. Such a limited number of working embodiments is clearly insufficient to enable the breadth of the claimed invention.

**6) The claims are of considerable breadth and encompass a large sundry list of structurally unrelated molecules (i.e., analogues, antibodies, peptidomimetics, small organic inhibitors, etc.) which receive inadequate support in the disclosure.** The broadest claims potentially encompass tens-of-thousands of unrelated compounds. However, the disclosure fails to lead the skilled artisan toward any particular structural class of related compounds.

**7) The state-of-the-art vis-à-vis the preparation of peptide analogues is associated with considerable unpredictability.** It has been well-documented that single amino acid substitutions, additions, or deletions can have profound and unpredictable effects on protein activity. Such modifications can completely abrogate peptide activity, have no bearing on said activity, or potentially enhance the activity (Hamelin *et al.*, 1993; Stepanova *et al.*, 1997). Unfortunately, the skilled artisan cannot determine *a priori* which analogues will have the desired activity.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention in a manner commensurate in scope with the claims.

*35 U.S.C. § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

*35 U.S.C. § 102(a)*

Claims 1-5 and 8 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Wada *et al.* (2001). Wada and colleagues provide compositions comprising the HMW-uPA and ATF fragment thereof, that are capable of inhibiting HIV-1 replication. Thus, this teaching meets all of the claimed limitations.

*35 U.S.C. § 119(a)-(d) and (f)*

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 C.F.R. § 1.55. See M.P.E.P. § 201.15.

*35 U.S.C. § 102(b)*

Claims 1-5 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stoppelli *et al.* (1985). Stoppelli and colleagues provide compositions comprising both the HMW-uPA and the amino terminal fragment (aa 1-135). These are the exact

same compounds currently being claimed by applicants. Accordingly, one of ordinary skill in the art would reasonably expect these compounds to inherently contain the same activities as applicants' claimed compounds.

*Correspondence*

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 9:30 AM to 7:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (571) 272-0910 or (571) 272-0902, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (571) 272-1600.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

21 March, 2004